copy of the pending claims is also submitted for the Examiner's convenience. The Applicants respectfully request the entry of these amendments. Claim 1 was amended to recite a proper antecedent basis for "said nucleic acid" by enclosing "cDNA or recombinant" in brackets.

Rejection under 35 U.S.C. § 101

Claims 1-2 & 4-7 stand rejected under 35 U.S.C. § 101 for lacking utility "because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility." Applicants respectfully traverse.

The Federal Circuit has stated, "[t]o violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result. MPEP § 2107.01 citing to" *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F. 2d 1555, 1571, 24 USPQ2d 1401, 1412 (Fed. Cir. 1992)(emphasis added). If an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on lack of utility is not appropriate. See *In re Brana*, 51 F. 3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995).

Rejections under 35 U.S.C. 101 have been rarely sustained by federal courts. Generally speaking, in these rare cases, the 35 U.S.C. 101 rejection was sustained either because the applicant failed to disclose any utility for the invention or asserted a utility that could only be true if it violated a scientific principle, such as the second law of thermodynamics, or a law of nature, or was wholly inconsistent with contemporary knowledge in the art. MPEP 2107.02 citing to, *In re Gazave*, 379 F. 2d 973, 978, 154 USPQ 92, 96 (CCPA 1967).

The claims of the present invention do not violate any scientific principle and Applicants have asserted a utility, namely that the nucleic acid sequence (SEQ ID No:1) of these novel homeodomain proteins, can be used to isolate sensory neurons. The fact that DRG11 is expressed in a very specific subset of sensory neurons, not expressed in sympathetic ganglia, and is expressed in the dorsal spinal cord but not the ventral spinal cord, gives this polynucleotide a specific function of identifying and/or isolating subsets of cells within a mixture that are a specific neuronal lineage separate and distinct from cells that do not express the DRG11 protein. See specification at page 31, lines 4-25. The DRG11 nucleic acid does not just act as a gene probe or

chromosome marker. Rather, additional utility lies in the fact that the unique expression pattern of DRG11 nucleic acids and protein can be exploited to identify specific subsets of cells within a neuronal lineage. This is a utility and therefore, the Applicant has not failed to disclose any utility and a rejection of the claimed invention as a whole based on lack of utility is not appropriate.

The Examiner states that

> Many proteins , or DNAs that encode such are expressed in sensory neurons, especially as it relates to the genus of hybridization products claimed, thereby not being a specific utility by definition.

Applicants respectfully disagree. It is true that DNAs that encode proteins other than DRG11are certainly expressed in sensory neurons. But these other nucleic acids are clearly distinct from the nucleic acids encoding for DRG11. For example, DRG11 nucleic acids are characterized by their ability to hybridize under high stringency conditions to the DRG11 nucleic acid of SEQ ID No:1. They also encode a DRG11 protein having significant sequence homology to known paired homeodomain transcription factors, but which lacks a paired domain as found in other homeodomain transcription factors (See Figure 4 and specification at page 29 lines 24-26; page 34 , lines 18-20). In addition, DRG11 ucleic acids are not expressed in non-neuronal cells, sympathetic neurons and ventricular neurons of the spinal cord. It is this subset of nucleic acids which define the genus of the DRG11 nucleic acids claimed.

The Examiner further states that further experimentation would be necessary before any "real world" utility can be attributed to the claimed polynucleotides. Applicants respectfully disagree.

Any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be sufficient, at least with regard to defining a "substantial" utility. See MPEP § 2107.02.

As provided above the unique expression pattern and known functionality of homeodomain transcription factors can be exploited in identifying specific subsets of cells. This would be considered by those of skill in the art to be a public benefit. In addition, although further experimentation would be necessary, the experimentation would not be considered undue and would be permissible, if it is merely routine, or if the specification in question provides a

reasonable amount of guidance with respect to the direction in which the experimentation should proceed. See MPEP § 2164.06, citing to *In re Wands*, 858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification in question does provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. The Examples explain how the cDNA was isolated (specification at page 28, lines 17-28; page 29, lines 1-15); the unique expression patterns observed through in situ hybridization studies (specification at page 30, lines 3-26, page31 and page 32, lines 1-16), together with the fact that DRG11 can be used as a molecular marker to identify neurons in the peripheral sensory lineage (specification at page 20, lines 5-8). This provides a reasonable amount of guidance so that one with ordinary skill in the art would understand the direction which the experimentation should proceed.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-2 and 4-7 were rejected under 35 U.S.C. § 112, first paragraph. The Examiner states "the reason for the rejection is since the claimed invention was found not to be supported by either a specific and/or substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention." For the reasons set forth above, the Applicants respectfully disagree.

Using a cloned sequence to identify specific cells within the sensory lineage is a specific utility. It is also a substantial utility as described above, since the use of this isolated cDNA would be considered a public benefit by those skilled in the art. It is also a well established utility since DRG11 sequence is a member of the homeodomain transcription factors, known to be important in development. The Examiner appears to state unless it is known where the DNA actually binds, then the utility requirement is not met. This is not the standard, even if the invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on a lack of utility is not appropriate. See *In re Brana*, 51 F. 3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). The claims to the present invention are directed to isolated cDNA encoding DRG11 (claim 1) and a method of expressing the protein in a transformed host cell (claim 7). Applicants have asserted a utility to meet 35 U.S.C. 101 utility requirement as

stated above, and hence the rejections based on 35 U.S.C. 101 or 35 U.S.C. 112, first paragraph are improper.

Therefore, Applicants respectfully requests the withdrawal of these rejections.

Claims 1 and 5-7 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. See, *Purdue Pharma L.P. v. Faulding Inc.*, 230 F. 3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) and MPEP § 2163 (II) (3).

As stated above, the sequence of the DRG11 cDNA is disclosed as SEQ ID No.:1. This nucleic acid encodes a DRG11 protein which lacks a paired domain and has a Gln instead of a Ser at position 9 of the recognition helix found in other homeodomain transcription factors (See residue 56 in Fig. 4 and specification at page 29, lines 24-26). In addition, the expression pattern of DRG11 nucleic acid is unique and specific to particular subsets of cells (and absent from other subsets of cells) as indicated by Southern blot analysis and in situ hybridization studies set forth in the examples beginning in specification at page 24-28 (lines 1-16) and page 30, lines 3-26 through page 32, lines 1-16. Further, the size of the isolated cDNA (2.4kb) (specification at page 29, lines 11-12) is another identifying characteristic which together with the above mentioned characteristics of the DRG11 sequence serve to provide sufficient evidence to inform the skilled artisan that the applicant was in possession of the claimed invention as a whole at the time the application was filed.

The Examiner goes on to state that

> one of ordinary skill in the art cannot visualize what generic nucleic acid sequences are specifically encompassed by the current claims, nor could one visualize what constitutes generic sequences encompassed by these claims based solely on the written description of the single cDNA sequence of SEQ ID NO:1 and because no

known or disclosed function exists for the encoded DRG11 protein(s) of the instant invention, what constitutes a functional allelic variant (as it relates to the hybridization products claimed) cannot be reasonably determined.

For the reasons mentioned above, the Applicants respectfully disagree.

One skilled in the art would be able to determine whether the cDNA isolated is the same as or different from the cDNA isolated by another by comparing sequence homology and expression patterns. Further, the instant claims are directed to isolated nucleic acid and a method of expressing the protein, not the protein itself as the Examiner appears to state. It is the function of the isolated cDNA as a marker for isolating specific subsets of sensory neurons and the unique expression pattern of the DRG11 protein that can also be exploited in identifying specific subsets of cells that is being claimed and this function is sufficient to overcome the 35 U.S.C. § 101 utility requirement. Further, one of ordinary skill in the art would understand the meaning of the use of making functional allelic variants as it relates to the hybridization products claimed, in making various predetermined mutations in the sequence of DRG11 and then comparing with wild type sequence effects such as but not limited to cell morphology and expression of various developmental markers. See specification at page 16, lines 6-27, pages 17-18. One of ordinary skill in the art could easily visualize cDNA or recombinant nucleic acid sequences that would (or would not) hybridize through base-pair complementarity under high stringency conditions with a nucleic acid having the specified sequence.

The Examiner cites to *Fiddes v. Baird*, 30 USPQ2d 1481, 1483 (1993) which held that claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class, in which the specification had provided an adequate description of only the bovine sequence. The Examiner then appears to analogize that since only the single species of the encoded rat DRG11 protein of SEQ ID NO:2, and its corresponding DNA of SEQ ID NO:1 has been described in the instant specification then, just as in *Fiddes v. Baird*, there is a lack of written description for the broad class of DRG11 cDNAs or recombinant nucleic acids.

The claims of the present invention can be distinguished from *Fiddes v. Baird* . In *Fiddes v. Baird*, only the amino acid sequence for bovine pituitary FGF was disclosed. The naturally

occurring nucleic acid FGF sequence was never obtained. See *Fiddes v. Baird*, 30 USPQ2d, 1481, 1485. Here, the Applicants have isolated and sequenced the DRG11 cDNA. In addition other identifying characteristics of the cDNA itself as mentioned above serve to sufficiently describe the members of the genus that would define a particular sequence as encoding a DRG11 protein.

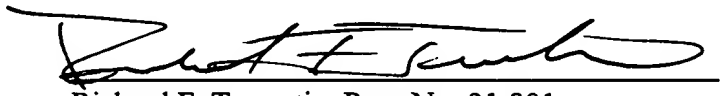
For the reasons discussed above, Claims 1, 2 and 4-7 sufficiently set forth an adequate written description of the cDNA or recombinant nucleic acid encoding a DRG11 protein and therefore, the rejection under 35 U.S.C. § 112, first paragraph is improper. Applicants respectfully request the withdrawal of the rejection.

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

FLEHR HOHBACH TEST
ALBRITTON & HERBERT LLP

Dated: April 17, 2002



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VERSION SHOWING CHANGES MADE

1. (Thrice Amended) An isolated cDNA or recombinant nucleic acid comprising a nucleic acid encoding a DRG11 protein, wherein said nucleic acid encoding a DRG11 protein hybridizes under high stringency conditions to a complement of a nucleic acid molecule having a sequence as set forth in SEQ ID NO:1, and wherein said DRG11 protein is characterized by its natural expression in sensory neurons and dorsal horn neurons of the spinal cord and wherein its natural expression is absent in non-neuronal cells, sympathetic neurons and ventricular neurons of the spinal cord.

2. (Twice Amended) An isolated nucleic acid according to claim 1 encoding the amino acid sequence depicted in Figure 3 (SEQ ID NO:2).

4. (Twice Amended) An isolated nucleic acid according to claim 1 comprising the nucleic acid depicted in Figure 2 (SEQ ID NO:1).

5. (Amended) An isolated nucleic acid according to claim 1 operably linked to an expression vector comprising transcriptional and translational regulatory DNA.

6. A host cell transformed with an expression vector according to claim 5.

7. (Amended) A method of producing a DRG11 protein comprising:

a) culturing a host cell transformed with an expression vector comprising a nucleic acid according to claim 1; and

b) expressing said nucleic acid to produce a DRG11 protein.

PENDING CLAIMS

1. (Thrice Amended) An isolated cDNA or recombinant nucleic acid comprising a nucleic acid encoding a DRG11 protein, wherein said nucleic acid encoding a DRG11 protein hybridizes under high stringency conditions to a complement of a nucleic acid molecule having a sequence as set forth in SEQ ID NO:1, and wherein said DRG11 protein is characterized by its natural expression in sensory neurons and dorsal horn neurons of the spinal cord and wherein its natural expression is absent in non-neuronal cells, sympathetic neurons and ventricular neurons of the spinal cord.

2. (Twice Amended) An isolated nucleic acid according to claim 1 encoding the amino acid sequence depicted in Figure 3 (SEQ ID NO:2).

4. (Twice Amended) An isolated nucleic acid according to claim 1 comprising the nucleic acid depicted in Figure 2 (SEQ ID NO:1).

5. (Amended) An isolated nucleic acid according to claim 1 operably linked to an expression vector comprising transcriptional and translational regulatory DNA.

6. A host cell transformed with an expression vector according to claim 5.

7. (Amended) A method of producing a DRG11 protein comprising:

a) culturing a host cell transformed with an expression vector comprising a nucleic acid according to claim 1; and

b) expressing said nucleic acid to produce a DRG11 protein.